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LETTERS AND CORRESPONDENCE

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Neonatal Intracranial Hemorrhage Secondary to Congenital Factor VII Deficiency: Two Case Reports

To the Editor: Congenital coagulation factor VII deficiency is a very rare disorder which is inherited as a highly penetrant, incompletely recessive autosomal trait [1]. The clinical severity of factor VII deficiency varies greatly, and hemorrhagic manifestations range from epistaxis to fatal intracranial bleeding. Here we report on 2 brothers who presented with massive intracranial bleeding in the neonatal period.

A term male infant was born via forceps delivery following an uncomplicated pregnancy. The parents were nonconsanguineous and there was no family history of hemorrhagic diasthesis. On the third day of life, the child developed seizures. A large intracerebral bleed was confirmed by CT scan of the brain. Coagulation studies showed that the child had a prolonged prothrombin time (PT), and factor VII assay was 5%. Normal studies included activated partial thromboplastin time (aPTT), thrombin time, platelet count, liver function tests, and creatinine. Fresh-frozen plasma was transfused, and cerebral resuscitation with ventilatory support was instituted. However, the child expired on day 20 of life, secondary to fulminant *Escherichia coli* sepsis.

Several months following the death of her first child, the mother conceived again. At term she underwent a cesarean section. A healthy 3-kg male infant was delivered with good Apgar scores. The child remained well till day 3 of life, when he developed spontaneous bleeding from the umbilical stump. He was also pale and had a tense anterior fontanelle. A left temporoparietal bleed was seen on CT scan of the brain. The PT ratio was 4.0, and aPTT was normal. Factor VII level was only 3%. Umbilical bleeding ceased, following transfusion of fresh-frozen plasma. Unfortunately, the child succumbed to *Staphylococcus aureus* septicemia on the twelfth day of life.

A family study demonstrated slightly reduced factor VII activity in the mother (73%). She was an adopted child, and no information regarding her biological family was available. Factor VII deficiency in the paternal family was found (Fig. 1).

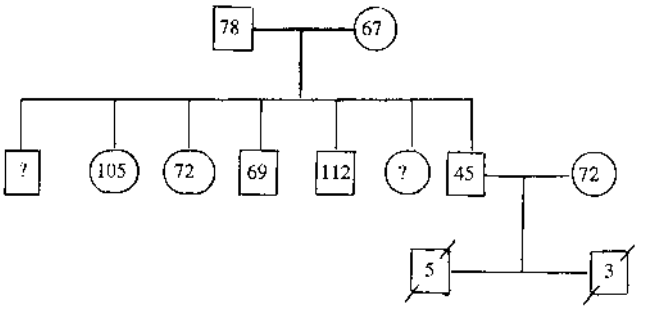

Fig. 1. Paternal family pedigree. Numbers indicate factor VII levels as percentage of normal. ?, not available for testing.

The 2 brothers in this case are most likely to be homozygous or compound heterozygous. In a review of 75 patients with proven factor VII deficiency, Ragni et al. [2] found 12 patients who developed CNS hemorrhage: an incidence of 16%. Five of these patients had intracranial bleeding prior to age 1 week, and none survived. The question of preventing hemorrhagic complications in the second child, as a positive family history was known, using "prophylactic" transfusion of plasma or factor VII concentrate, remains conjectural. The literature on neonatal factor VII deficiency is scant, and the decision to give a human blood product or factor VII concentrate cannot be justified in a nonbleeding patient, especially as the risk of infection from blood-borne viruses cannot be entirely excluded.

We feel that "prophylactic" measures in the management of these cases should involve efforts to diagnose the disease antenatally and, thus, complications can be anticipated based on objective data. The gene for factor VII has been located on the long arm of chromosome 13 [3]. In 1992, Millar et al. [4] reported the first successful exclusion of factor VII deficiency in an at-risk pregnancy, using DNA sequencing on chorionic villous material obtained in the tenth week of pregnancy.

In conclusion, we suggest that management of similar cases should begin with the detection or exclusion of this disease in utero. The value of replacing factor VII in deficient patients who are asymptomatic remains unproven.

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REFERENCES

1. Alexander B, Goldstein R, Landwehr G, Cook CD: Congenital SPCA (factor VII) deficiency: A hitherto unrecognised coagulation defect with haemorrhage rectified by serum and serum fractions. J Clin Invest 30:596, 1951.
2. Ragni MV, Lewis JH, Spero JA, Hasiba U: Factor VII deficiency. Am J Haematol 10:79–88, 1981.
3. McKusick VA: The morbid anatomy of the human genome. A review of gene mapping in clinical medicine. Medicine (Baltimore) 66:237–296, 1987.
4. Millar DS, Cooper DN, Kakkar VV: Prenatal exclusion of severe factor VII deficiency by DNA sequencing. Lancet 339:1359, 1992.